

I claim:

1. A peptide immunogen of about 20 to 100 amino acids long comprising:
  - (i) a helper T cell (Th) epitope selected from the group consisting of SEQ ID Nos: 1 to 64;
  - (ii) an N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide, SEQ ID NO:65, consisting of from 10 to 28 amino acid residues wherein each fragment comprises amino acid residue 1 of the A $\beta$ <sub>1-42</sub> peptide or an immunologically functional analog of the N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide; and
  - (iii) optionally a spacer consisting of at least an amino acid to separate the immunogenic domains.
2. A peptide immunogen of claim 1, wherein the spacer is selected from the group consisting of an amino acid, Gly-Gly, ( $\alpha$ ,  $\epsilon$ -N)-Lys, and Pro-Pro-Xaa-Pro-Xaa-Pro (SEQ ID NO:73).
3. A peptide immunogen of claim 2, wherein the spacer is Gly-Gly.
4. A peptide immunogen of claim 2, wherein the spacer is  $\epsilon$ -N-Lys.
5. A peptide immunogen of claim 1, wherein the N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide is selected from the group consisting of SEQ ID NOs: 66-69 and an immunologically functional analog thereof.
6. A peptide immunogen of any one of claims 2, 3, or 4, wherein the N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide is selected from the group consisting of SEQ ID NOs: 66-69 and an immunologically functional analog thereof.

7. A peptide immunogen of claim 1, wherein Th is selected from the group consisting of SEQ ID NOs: 1, 3, 4, 5, 6, 7, 8, 9, 20, 38-40, 47-51 and 52-54.
8. A peptide immunogen of any one of claims 2, 3, or 4, wherein Th is selected from the group consisting of SEQ ID NOs: 1, 3, 4, 5, 6, 7, 8, 9, 20, 38-40, 47-51 and 52-54..
9. A peptide immunogen selected from the group consisting of SEQ ID NOs: 70, 71, 72, 73, and 74.
10. A peptide immunogen of claim 9 consisting of SEQ ID NO: 73.
11. A peptide immunogen of claim 9 consisting of SEQ ID NO: 74.

12. The peptide immunogen represented by one of the following formulae:

<sup>6-10</sup> (A)<sub>n</sub>-(N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide)-(B)<sub>o</sub>-(Th)<sub>m</sub>-X; or  
 (A)<sub>n</sub>-(Th)<sub>m</sub>-(B)<sub>o</sub>-(N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide)-X;

wherein

each A is independently an amino acid;

each B is a linking group selected from the group consisting of an amino acid, gly-gly, ( $\alpha$ ,  $\epsilon$ -N)-Lys, and Pro-Pro-Xaa-Pro-Xaa-Pro (SEQ ID NO:73);

Th comprise an amino acid sequence that constitutes a helper T cell epitope, selected from the group consisting of SEQ ID NOs: 1-64 and an immune enhancing analog thereof;

(N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide) is 10 to about 28 amino acid residues and wherein each fragment comprises EFRH of the A $\beta$ <sub>1-42</sub> peptide and immunologically functional analog thereof;

X is an  $\alpha$ -COOH or  $\alpha$ -CONH<sub>2</sub> of an amino acid ;

n is from 0 to about 10;

m is from 1 to about 4; and

o is from 0 to about 10.

- 
13. A peptide immunogen of claim 12, wherein the spacer is Gly-Gly.
14. A peptide immunogen of claim 12, wherein the spacer is  $\epsilon$ -N-Lys.
15. A peptide immunogen of claim 12, wherein the N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide is selected from the group consisting of SEQ ID NOs: 66-69 and an immunologically effective analog thereof.
16. A peptide immunogen of any one of claims 13, or 14 , wherein the N-terminal fragment of A $\beta$ <sub>1-42</sub> peptide is selected from the group consisting of SEQ ID NOs: 66-69 and an immunologically functional analog thereof
17. A peptide immunogen of claim 12, wherein Th is selected from the group consisting of SEQ ID NOs: 1, 3, 4, 5, 6, 7, 8, 9, 20, 38-40, 47-51 and 52-54..
18. A peptide immunogen of any one of claims 13, or 14 wherein Th is selected from the group consisting of SEQ ID NOs: 1, 3, 4, 5, 6, 7, 8, 9, 20, 38-40, 47-51 and 52-54.
19. A peptide immunogen of claim 15 wherein Th is selected from the group consisting of SEQ ID NOs: 1, 3, 4, 5, 6, 7, 8, 9, 20, 38-40, 47-51 and 52-54.
20. A peptide immunogen of claim 16 wherein Th is selected from the group consisting of SEQ ID NOs: 1, 3, 4, 5, 6, 7, 8, 9, 20, 38-40, 47-51 and 52-54.

21. A composition comprising a peptide immunogen of claim 1 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
22. A composition comprising a peptide immunogen of claim 2 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
23. A composition comprising a peptide immunogen of claim 3 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
24. A composition comprising a peptide immunogen of claim 4 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
25. A composition comprising a peptide immunogen of claim 5 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.

26. A composition comprising a peptide immunogen of claim 6 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
27. A composition comprising a peptide immunogen of claim 7 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
28. A composition comprising a peptide immunogen of claim 8 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
29. A composition comprising a peptide immunogen of claim 9 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
30. A composition comprising a peptide immunogen of claim 10 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.

APP.  
2/1/00

31. A composition comprising a peptide immunogen of claim 11 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
32. A composition comprising a peptide immunogen of claim 12 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720
- ~~33.~~ A composition comprising a peptide immunogen of claim 13 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
34. A composition comprising a peptide immunogen of claim 14 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
35. A composition comprising a peptide immunogen of claim 15 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.

36. A composition comprising a peptide immunogen of claim 16 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
37. A composition comprising a peptide immunogen of claim 17 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
38. A composition comprising a peptide immunogen of claim 18 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
39. A composition comprising a peptide immunogen of claim 19 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.
40. A composition comprising a peptide immunogen of claim 20 and a pharmaceutically acceptable adjuvant and/or carrier selected from the group consisting of alum, liposyn, saponin, squalene, L121, emulsigen monophosphoryl lipid A (MPL), polysorbate 80, QS21, Montanide ISA51, ISA35, ISA206 and ISA 720.

41. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 21.
42. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 22.
43. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 23.
44. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 24.
45. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 25.
46. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 26.
47. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 27.
48. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 28.
49. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 29.
50. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 30.

51. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 31.
52. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 32.
53. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 33.
54. A method of preventing Alzheimer's disease by administering to a mammal a composition of claim 34.
55. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 35.
56. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 36.
57. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 37.
58. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 38.
59. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 39.
60. A method of preventing or treating Alzheimer's disease by administering to a mammal a composition of claim 40.

61. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 21.
62. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 22.
63. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 23.
64. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 24.
65. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 25.
66. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 26.
67. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 27.

68. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 28.
69. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 29.
70. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 30.
71. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 31.
72. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 32.
73. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 33.
74. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 34.

006654-05501  
105250-4625360

75. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 35.
76. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 36.
77. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 37.
78. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 38.
79. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 39.
80. A method of producing antibodies to A $\beta$ <sub>1-42</sub> peptide that is cross reactive to soluble A $\beta$  peptides and brain tissue plaques formed therefrom by administering a composition of claim 40.